CLAIMS

1. An *in vitro* method for increasing the synthesis of extracellular matrix compounds in a cell population by inhibiting the expression of IL1RI characterised in that it comprises the step of contacting the cells with an IL1RI exon-bridging antisense oligomer.

2. The method of claim 1, wherein said IL1R1 exon-bridging antisense oligomer is complementary to a sequence bridging exons 02-03 in the mature mRNA of the IL1R1 gene.

3. The method of claim 1 or 2, wherein said IL1R1 exon-bridging antisense oligomer comprises a sequence between 15 and 30 nucleotides and does not comprise a sequence of more than 11 consecutive nucleotides which are complementary to the sequence at the 3' end or the sequence at the 5' end of the exon-exon boundary in the mature mRNA of the IL1R1 gene.

4. The method of any one of claims 1 to 3, wherein said IL1R1 exon-bridging antisense oligomer is selected from a group consisting of probe NO: 6 (SEQ ID NO:6), probe NO:7 (SEQ ID NO:7), probe NO:8 (SEQ ID NO:8), probe NO:21 (SEQ ID NO:21) or a sequence having at least 70% sequence identity with the complementary sequence of the cDNA of the IL1R1 gene corresponding to probes NO:6, NO:7, NO:8 or probe NO:21.

5. The method of any one of claims 1 to 4, wherein said IL1R1 exon-bridging antisense oligomer comprises SEQ ID NO:7.

6. The method of claim 1, wherein said IL1R1 exon-bridging antisense oligomer is complementary to a sequence bridging exon 05-06 of the mature mRNA of the IL1R1 gene.

7. The method of claim 6, wherein said IL1R1 exon-bridging antisense oligomer is selected from a group consisting of probe NO: 24 (SEQ ID NO:24) or a

sequence having at least 70% sequence identity with the complementary sequence of the cDNA of the IL1R1 gene corresponding to probe NO:24.

8. An antisense oligomer for the inhibition of the expression of IL1RI characterised in that said antisense oligomer is an exon-bridging antisense oligomer.

9. The antisense oligomer of claim 8, which is complementary to a sequence bridging exons 02-03 of the mature mRNA of the IL1R1 gene.

10. The antisense oligomer of claim 8 or 9, which comprises a sequence between 15 and 30 nucleotides and does not comprise a sequence of more than 11 consecutive nucleotides which are complementary to the sequence at the 3' end or the sequence at the 5' end of the exon-exon boundary in the mature mRNA of the IL1R1 gene.

11. The antisense oligomer of any one of claims 8 to 10, wherein said IL1R1 exon-bridging antisense oligomer is selected from a group consisting of probe NO: 6 (SEQ ID NO:6), probe NO:7 (SEQ ID NO:7), probe NO:8 (SEQ ID NO:8), probe NO:21 (SEQ ID NO:21) or a sequence having at least 70% sequence identity with the complementary sequence of the cDNA of the IL1R1 gene corresponding to probes NO:6, NO:7, NO:8 or SEQ ID NO:21.

12. The antisense oligomer of any one of claims 8 to 11, wherein said IL1R1 exon-bridging antisense oligomer comprises SEQ ID NO:7.

13. The antisense oligomer of claim 8, which is complementary to a sequence bridging exons 05-06 of the mature mRNA of the IL1R1 gene.

14. The antisense oligomer according to claim 13, wherein said IL1R1 exon-bridging antisense oligomer comprises SEQ ID NO:24.

15. The antisense oligomers of any one of claims 8 to 14 for use as a medicament.

16. A pharmaceutical composition comprising one or more antisense oligomers according to any one of claims 8 to 14 for the inhibition of the expression of IL1R1 and further comprising at least one pharmaceutically acceptable carrier.

17. The use of one or more antisense oligomers according to any one of claims 8 to 14 for the preparation of a medicament for the treatment or prevention of a disease characterized by a cartilage or osteochondral defect.

18. The use of claim 17 wherein said disease is osteoarthritis.

19. The use of one or more antisense oligomers according to any one of claims 8 to 14 for the preparation of a medicament for the treatment or prevention of a disease selected from the group consisting of neuropathies, such as diabetic neuropathy, immune-mediated damage to the peripheral nervous system, heat hyperalgesia, Guillain-Barre syndrome, AIDS, bone disorders, such as osteoporosis caused by lymphomyeloid proliferative diseases, bone resorption, as occurring in a variety of diseases including osteoporosis, periodontal disease and rheumatoid arthritis, atheromatosis, coronary heart diseases, acute renal failure, asthma and nasal polyposis.

20. A method for the *in vitro* modulation of the expression of a target gene in a cell population with an antisense oligomer said method characterised in that mature mRNA function is inhibited by contacting the cells with an exon-bridging antisense oligomer directed against said mature mRNA.

21. The method of claim 20, wherein said exon-bridging antisense oligomer has a length of between 15-30 nucleotides.

22. The method according to claim 20 or 21, wherein the step of contacting the cells is performed in the absence of a DNA transfecting agent.

23. The method according to any one of claims 20 to 22, wherein the function of all mature mRNAs originating from said target gene is inhibited.

24. The method according to any one of claims 20 to 23, wherein the target gene is Interleukin 1 Receptor type I (IL1RI).

25. The method according to any one of claims 20 to 24, wherein the complementary sequence of said exon-bridging antisense oligomer has less than 70% sequence identity with a nucleotide sequence other than the mature mRNA or DNA of said target gene.

26. The method according to claim 20, wherein said exon-bridging antisense oligomer has a GC content of at least 45%.

27. The method according to any one of claims 20 to 26, wherein the sequences complementary to the 5' and 3' end of the exon-exon boundary of said mRNA of said target gene have a Tm of less than 32-36°C.

28. The method according to any one of claims 20 to 27, wherein said exon-bridging antisense oligomer does not comprise a sequence of more than 11 consecutive nucleotides which are complementary to the sequence at the 3' end or the sequence at the 5' end of the exon-exon boundary in the mature mRNA of the target gene.

29. The method of any one of claims 20 to 28, wherein the sequence of said exon-bridging antisense oligomer sequence has at least 70 % sequence identity with the complementary sequence of the cDNA of said target gene.

30. The method according to any one of claims 20 to 29, which comprises contacting said cells with 1 to 100 nM of said exon-bridging antisense oligomer.

31. The method according to any one of claims 20 to 29, which comprises contacting said cells with 1 to 10 nM of said exon-bridging antisense oligomer.

32. The method according to any one of claims 20 to 31, wherein said cells are chondrocytes, chondrocyte precursors, fibrochondrocytes, or fibroblasts.

33. The method according to any one of claims 20 to 31, wherein said cells are osteoarthritic chondrocytes.

34. A method for producing an exon-bridging antisense oligomer for the inhibition of expression of a target gene comprising the steps of:

1) determining the exon-exon boundaries in the sequence of a spliced mRNA of said target gene,

2) selecting a sequence with a length between 15 and 30 residues bridging an exon-exon boundary in the spliced mRNA of said target gene, said sequence comprising at its 5' end or 3' end at least 4 residues identical to a sequence 5' of said exon-exon boundary and, optionally said sequence comprising at its 3' or 5' end a maximum of 11 residues identical to the sequence 3' adjacent of said exon-exon boundary.

3) producing an antisense oligomer which consists of a sequence which is has at least 70% sequence identity with a sequence complementary to the sequence selected in step 2.

35. A method according to claim 34 further wherein step 2 further comprises one or more of the steps selected from the group consisting of:

a) determining whether the GC content of said sequence determined under (2) is above 45 %,

b) determining whether the Tm of each of the sequences 3' and 5' of the exon-exon boundary within said sequence is below 32-36°C,

c) determining whether said oligomer has a sequence identity below 70% with mature mRNA other than the mature mRNA or DNA of the target gene;

And selecting the one or more sequences which fulfil the criteria of one or more of steps a to c.

36. A method of treatment for a disease characterized by the overexpression of IL1R1, which comprises administering to a patient an exon-bridging antisense probe directed to mature mRNA of IL1R1.

37. An *in vitro* method for increasing the synthesis of extracellular matrix compounds in a cell population by inhibiting the expression of IL1RI characterised in that it comprises the use of sequences complementary to the sequences bridging two coding exons in the cDNA of IL1R1.